JPW

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To: JOHN P. WHITE
COOPER AND DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK NY 10036

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	25 OCT 2001
IMPORTANT NOTIFICATION	

Applicant's or agent's file reference	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
59338-B-PCT	26 MAY 2000	28 MAY 1999
International application No. PCT/US00/14654		

Applicant
SYNAPTIC PHARMACEUTICAL CORPORTATION

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

11/28/01 W.D.

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer FOZIA HAMUD
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/416 (July 1992)*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 59338-B-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/14654	International filing date *(day/month/year)* 26 MAY 2000	Priority date *(day/month/year)* 28 MAY 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant SYNAPTIC PHARMACEUTICAL CORPORTATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets.

   [✓] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [X] Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV [X] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [X] Certain observations on the international application

Date of submission of the demand 15 DECEMBER 2000	Date of completion of this report 26 SEPTEMBER 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer FOZIA HAMUD Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/14654

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed

☒ the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the claims:
pages (See Attached) , as originally filed
pages _____ , as amended (together with any statement) under Article 19
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the drawings:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the sequence listing part of the description:
pages (See Attached) , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/14654

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. (Please See supplemental sheet)

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. (See Attached) .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/14654

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- [ ] restricted the claims.
- [ ] paid additional fees.
- [ ] paid additional fees under protest.
- [ ] neither restricted nor paid additional fees.

2. [X] This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- [ ] complied with.
- [X] not complied with for the following reasons:

Please See Supplemental Sheet.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- [ ] all parts.
- [X] the parts relating to claims Nos. (Please See supplemental sheet).

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/14654

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. citations and explanations (Rule 70.7)

Claims 38-39, 42, 45 and 102 lack novelty under PCT Article 33(2) as being anticipated by EP 859,0551 A1 (SMITHKLINE BEECHUM CORP). EP 859,0551 document teaches an isolated polynucleotide encoding a G-protein coupled receptor,(see abstract and claims). The polynucleotide disclosed in this reference has a 28.5% homology to the polynucleotide with SEQ ID NO:5 of the present invention. See the copy of the comparison of SEQ ID NO:5 claimed in the instant invention and the sequence of the reference (SEQUENCE COMPARISON 'A'). Therefore, in the absence of recitation of the stringency conditions in claims 38-39, 42, 45 and 102 the polynucleotide taught by the EP 859,0551 reference would hybridize to the instant claimed polynucleotide of SEQ ID NO:5.

Claims 38-39, 42, 45 and 102 lack novelty under PCT Article 33(2) as being anticipated by EP 859,0551 A1 (The University of Sheffield). GB 2312211 A document teaches olignucleotides encoding human H2 receptor,(see abstract and SEQ ID NO:2 on pages 25-28). The olignucleotide disclosed in this reference has a 8.2% homology to the polynucleotide set forth in SEQ ID NO:5 of the present invention. See the copy of the comparison of SEQ ID NO:5 claimed in the instant invention and the sequence of the reference (SEQUENCE COMPARISON 'B'). Therefore, in the absence of recitation of the stringency conditions in claims 38-39, 42, 45 and 102 the polynucleotide taught by the GB 2312211 A reference would hybridize to the instant claimed polynucleotide of SEQ ID NO:5.

Claims 1-9, 16-17, 19-25, 28-32, 35-36, 45-46, 118-119, 66-72, 77-87, 89-97, 99-101, 120-154, 159-168 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest an isolated nucleic acid encoding a human SNORF33 receptor with the amino acid sequence set froth in SEQ ID NO:6, said nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:5 or a method of identifying compounds that specifically bind to said human SNORF33 receptor.

Claims 1-9, 16-17, 19-25, 28-32, 35-39, 42, 45-46, 66-72, 77-87, 89-97, 99-102, 118-154, 159-168 lack industrial applicability as (Continued on Supplemental Sheet.)

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to adequately enable practice of the claimed invention because: the description fails to provide an enabling disclosure for claims that are drawn to "all" possible mammalian or human "snorf33" receptors. The description is enabling for an isolated nucleic acid comprising the polynucleotide sequence set forth in SEQ ID NO:5, encoding the polypeptide of SEQ ID NO:6, and a method of identifying compounds that bind to said polypeptide. The disclosure of the polynucleotide of SEQ ID NO:5 and the encoded receptor does not enable the skilled artisan to make and use all possible mammalian and human snorf33 receptors.

Claims 1-5, 16-17, 1-25, 28-32, 35-37, 45-46, 102, 118-119, 66-67, 77-96, 99-101 and 120-168 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

CLASSIFICATION:
The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/12, 5/10; C12P 21/02; C07K 14/47, 14/705; G01N 33/53, 33/566, 33/567 and US Cl.: 435/69.1, 7.1, 7.2, 7.21, 71.1, 320.1, 471, 325, 334, 358, 361, 365, 368, 252.3, 255.1; 536/23.5; 530/350

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
page(s) 1-53, 55-197, as originally filed.
page(s) 54, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
page(s) 198-200, 202-229, as originally filed.
page(s) none, as amended under Article 19.
page(s) 201, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the drawings,
page(s) 1-28, as originally filed.
page(s) NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the sequence listing part of the description:
page(s) 1-18, as originally filed.
pages(s) NONE, filed with the demand.
and additional amendments:
NONE

III. NON-ESTABLISHMENT OF REPORT:

The questions of whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect to claim numbers 10-15, 18, 26-27, 33-34, 40-41, 43-44, 47-65, 73-76, 88, 98, 103-117, 155-158.

No international search report has been established for claim numbers 10-15, 18, 26-27, 33-34, 40-41, 43-44, 47-65, 73-76, 88, 98, 103-117, 155-158.

4. The parts of the international application relating to claim-87, 99-102, 118-154, 159-168 were the subject of international

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

number(s) 1-9, 16-17, 16-17, 19-25, 35-39, 42, 45-46, 66-72, 77 preliminary examination in establishing this report.

V. 1. REASONED STATEMENTS:
The report as to Novelty was positive (YES) with respect to claims 1-9, 16-17, 25-32, 35-36, 45-46, 118-119, 66-72, 77-87, 89-97, 99-101, 120-154, 159-168.
The report as to Novelty was negative (NO) with respect to claims 38-39, 42, 45, 102.
The report as to Inventive Step was positive (YES) with respect to claims 1-9, 16-17, 19-25, 28-32, 35-37, 45-46, 118-119, 66-72, 77-87, 99-101, 120-154, 159-168.
The report as to Inventive Step was negative (NO) with respect to claims 38-39, 42, 45, 102.
The report as to Industrial Applicability was positive (YES) with respect to claims none.
The report as to Industrial Applicability was negative (NO) with respect to claims 1-9, 16-17, 19-25, 28-32, 35-39, 42, 45-46, 66-72, 77-87, 88-97, 99-102, 118-154, 159-168 .

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
defined by PCT Article 33(4). The polynucleotides and the polypeptides of instant claims are "orphans" in that no known biological activity has been attributed to them. There is little doubt that, after complete characterization, the instant polynucleotide of SEQ ID NO:5 and the encoded protein may be found to have a specific, substantial and credible utility. Thus, further characterization, is part of the act of invention and until it has been undertaken, the claimed invention is incomplete. The instant claims are directed to polynucleotide encoding a human SNORF33 receptor and methods of identifying compounds that bind to said receptor, however, there is no biological function or significance for these polypeptides or the polynucleotides encoding them, therefore, compounds that bind to said receptor would have no biological significance or utility. The description indicates that instant h SNORF33 receptor is an orphan G-protein coupled receptor, but there is no disclosure ad to the biological significance or any functional characteristics of this receptor and the polynucleotide encoding it. Until some actual and specific significance can be attributed to the claimed polynucleotide and the encoded receptor, the instant invention is incomplete and does not possess industrial applicability. Since the description does not disclose a credible and "real world" use for the hSNORF33 receptor or the nucleic acid encoding it or compounds that bind to it, the claimed invention is incomplete and does not have industrial applicablity.

---------- NEW CITATIONS ----------
NONE

26. The plasmid of claim 23 designated pcDNA3.1-rSNORF33-f (ATCC Patent Depository No. PTA-102).

27. The plasmid of claim 23 designated pEXJ-mSNORF33-f (ATCC Patent Depository No. PTA-1665).

28. A cell comprising the vector of claim 21.

29. A cell of claim 28, wherein the cell is a non-mammalian cell.

30. A cell of claim 29, wherein the non-mammalian cell is a *Xenopus* oocyte cell or a *Xenopus* melanophore cell.

31. A cell of claim 28, wherein the cell is a mammalian cell.

32. A mammalian cell of claim 31, wherein the cell is a COS-7 cell, a 293 human embryonic kidney cell, a NIH-3T3 cell, a LM(tk-) cell, a mouse Y1 cell, or a CHO cell.

33. The CHO cell of claim 32 designated CHO-ratSNORF33-7 (ATCC Patent Depository No. PTA-1807).

34. The 293 cell of claim 32 designated 293-ratSNORF33-31 (ATCC Patent Depository No. PTA-1806).

35. A cell of claim 24, wherein the cell is an insect cell.

36. An insect cell of claim 29, wherein the insect cell is

is a *Xenopus* oocyte cell or a *Xenopus* melanophore cell. In another embodiment, the cell is a mammalian cell. In another embodiment, the cell is a COS-7 cell, a 293 human embryonic kidney cell, a NIH-3T3 cell, a LM(tk-) cell, a mouse Y1 cell, or a CHO cell. In another embodiment, the cell is an insect cell. In another embodiment, the insect cell is an Sf9 cell, an Sf21 cell or a Trichoplusia ni 5B-4 cell.

In one embodiment, the mammalian cell line is the 293 cell line designated 293-ratSNORF33-31. This cell line was deposited on May __, 2000, with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, Virginia 20110-2209, U.S.A. under the provisions of the Budapest Treaty for the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, and was accorded _____.

In another embodiment, the mammalian cell line is the CHO cell line designated CHO-ratSNORF33-7. This cell line was deposited on May __, 2000, with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, Virginia 20110-2209, U.S.A. under the provisions of the Budapest Treaty for the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, and was accorded _____.

This invention provides a membrane preparation isolated from the cell in accordance with this invention.

Furthermore, this invention provides for a nucleic acid